HFI-35 M929N

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Refer to: 1121753

Baltimore District
900 Madison Avenue
Baltimore, Maryland 21201
Telephone: (410) 962-4040

May 21, 1997

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Ovila J. Dionne, President
Nucletron Corporation
7080 Columbia Gateway Drive
Columbia, Maryland 21046-2133

Dear Mr. Dionne:

The Food and Drug Administration (FDA) conducted an inspection of your firm and the affiliated Research and Development Department located in Columbia, Maryland, between February 3, 1997 and March 24, 1997. Our investigator(s) determined that your firm manufactures the Veriflex hardware and software system, and imports and distributes catheters, ring applicators, and other brachytherapy system products. These products are devices as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The inspection revealed that these devices are adulterated within the meaning of Section 501(h) of the Act, in that the methods used in, or the facilities or controls used for, manufacturing, packing, storage, or installation are not in conformance with the Good Manufacturing Practice (GMP) for Medical Devices Regulation, Title 21, Code of Federal Regulations (CFR), Part 820, as follows:

1. Failure to follow written MDR procedures. For example, three MDRs classified as being related to death, serious injury, or hazard to safety were not submitted to FDA as required by your internal SOP MDR-803-01. Six MDRs classified as "Severe" were not submitted to FDA as required by your Corrective and Preventative Action SOP.

2. Failure to follow written complaint procedures; to fully investigate a device's failure to meet performance specifications after it has been released for distribution; and to make a written record of the investigation, including conclusions and follow-up. For example, for 18 complaints, there were either no complaint report forms as required by SOPs, incomplete failure investigations, or lack of documentation indicating what corrective actions were taken, if any.

3. Failure to maintain, follow, document, or control component acceptance. For example:

   a. Sterile catheters which did not meet specifications were received, accepted, and placed into inventory. This failure to meet specifications was not reported to management as required by SOPs.

   b. Specific versions of Veriflex software are ordered, but no SOPs exist which require verification of the version received. Furthermore, the Purchase Order database, used to check incoming components against part numbers, lists obsolete software versions under the current part number.

   c. Defective components were not removed from the accepted product inventory. For example, flexiguide cone catheters (part numbers 083.286/276), which were tested and found to break easily in August of 1996, were still in the accepted product inventory as of March 11, 1997.

4. Failure to assure that personnel are trained to perform their assigned responsibilities. For example, there was no documentation to show that the employees responsible for the receipt, review and acceptance of incoming components, such as sterile catheters, had ever been trained in the "Handling of Sterile Products" SOP. Also, there was no documentation to show that employees responsible for staging of Veriflex Systems were trained in the installation SOPs.

5. Failure to maintain a complete Master Device Record for the Veriflex system. For example, there are no specific written procedures to indicate what specific steps are required for a system upgrade versus a completely new system installation, or who is responsible for which steps and where they are to be performed.

6. Failure to follow procedures for the installation of Veriflex systems. For example, the approved installation SOP and forms #VFX622/8003/951130, dated 11/30/95, were changed without approval when the Veriflex system at the [redacted] was upgraded.

7. Failure to maintain a complete Master Device Record, in that the approved Veriflex Installation Instructions do not match the Veriflex System Requirement Specifications for version 2.03c.

8. Failure to maintain a complete Device History Record. For example, Veriflex systems were installed or upgraded at seven user sites, no documentation was available to show that this work had been conducted per the approved installation instructions dated 11/30/95. Also, the current approved Acceptance Protocol #109.503 was not used during the Veriflex installations at [redacted].

With regard to the affiliated Research and Development Department located at your facility, the following practices do not comply with GMP requirements:

1. Failure to maintain complete Master Device Records. For example, there were no approved written system requirement specifications for Veriflex versions 2.02 and 2.04. Also, the system requirement specifications for Veriflex version 2.03c do not match the system specifications in the Installation SOPs for either versions 2.03c or 2.04.

2. Failure to have portions of the Veriflex Master Device Record and changes to the Master Device Record signed by designated individuals. For example, Transfer Reports for Veriflex versions 2.01, 2.02, 2.03, and 2.04 were not signed by all designated individuals..

3. Failure to follow complaint procedures and to maintain complete complaint files, as the files did not always contain required documentation or the reply to the complainant. For example, complaints involving errors in Veriflex software are fixed and reported to customers in technical bulletins for the next released version of the software. However, not all complaints resolved by a particular version of the software are reported to the customers in these technical bulletins. For example, complaint report 30-951200101 was corrected in Veriflex version 2.02, but was not reported to the customers in the technical bulletin for version 2.02.

4. Failed to maintain complete written failure investigation records, including records of the investigation, conclusions, and follow-up regarding Veriflex system software failures to meet performance specifications after the device had been released for distribution. For example, the "Test Plans" for the validation of Veriflex software corrections do not correspond to the "Test Cases" and complaint numbers in the "Test Reports."

5. Failure to perform adequate finished product testing for Veriflex version 2.05, in that the software testing for this version did not fully test the software under simulated

conditions of use. For example, the software testing to correct the software errors covered by Device Complaint Report #30-163, "Continuous log printing not printing wedge MU's" covered only expected operational conditions. There was no testing of error conditions, negative testing, or boundary condition testing.

Additionally, the above referenced inspection revealed that your devices are misbranded within the meaning of Section 502(t)(2) of the Act, in that your firm failed to submit information to the FDA as required by the Medical Device Reporting (MDR) regulation, as specified in 21 CFR Part 803. Specifically, you failed to submit malfunction MDR reports to FDA after receiving information which reasonably suggested that one of your commercially distributed devices had malfunctioned and could have caused or contributed to a death or serious injury if the malfunction recurred. An MDR malfunction report is required for 96-C016 and 96-C018. There should be a separate MDR report for each complaint in 96-C016. Please submit MDR reports to:

Mrs. Brenda S. Lucas, RN, BSN, Med
Reporting Systems Monitoring Team (HFZ-533)
Food and Drug Administration
Division of Surveillance and Biometrics
Center for Devices and Radiological Health
1350 Piccard Drive
Rockville, Maryland 20850

Nucletron Corporation should also review its SOPs regarding the criteria for determining the reportability of an adverse event.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA 483 issued at the closeout of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

To facilitate FDA in determining that such corrections have been made, we are requesting that you submit to this office, on the schedule below, certification by an outside expert consultant that they have conducted an audit of your firm's manufacturing and quality assurance systems relative to the requirements of the device GMP regulation (21 CFR, Part 820). This certification should enable FDA to: (1) withdraw its advisory to other federal agencies concerning the award of government contracts, and (2) resume marketing clearance and export clearance for products manufactured at your Columbia, Maryland facility. You should also

submit a copy of the consultant's report and certification by your firm's CEO (if other than yourself) that he or she has reviewed said report and that your firm has initiated or completed all corrections called for in the report. The enclosed guidance may be helpful in selecting an appropriate consultant.

The initial certifications of audit and corrections and subsequent certifications of updated audits and corrections (if required) should be submitted to this office by the following dates:

- Initial certifications by consultant and firm - November 21, 1997
- Subsequent certifications - November 21, 1998 and November 21, 1999

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, no pre-market submissions for devices to which the GMP deficiencies are reasonably related will be cleared until the violations have been corrected. Also, no requests for Certificates for Products for Export will be approved until the violations related to the subject devices have been corrected.

You should take prompt action to correct these deviations. Failure to do so may result in regulatory action being initiated by the FDA without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

Please notify this office in writing within 15 working days of receipt of this letter of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to identify and make corrections to any underlying systems problems necessary to assure that similar violations will not recur. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Your response should be sent to Gerald W. Miller, Compliance Officer, U.S. Food and Drug Administration, 101 West Broad Street (Suite 400), Falls Church, Virginia 22046-4200.

Sincerely yours,

Peter M. Dubinsky
Acting Director, Baltimore District

Enclosure